

## Claims

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1. An apparatus for marking a specimen, the apparatus comprising:  
an optical instrument;  
a marker coupled to the optical instrument and disposed outside a field of view of the optical instrument; and  
a stage coupled to the optical instrument for receiving the specimen and moving the specimen between an inspection position in an optical path of the optical instrument and a marking position for marking the specimen with the marker.
  2. The apparatus of claim 1, wherein the optical instrument comprises:  
a nosepiece;  
an illumination source; and  
focusing optics.
  3. The apparatus of claim 2, wherein the optical instrument is in data communication with a computer.
  4. The apparatus of claim 3, wherein the nosepiece comprises at least one lens.
  5. The apparatus of claim 4, wherein the at least one lens comprises a 10X objective.
  6. The apparatus of claim 5, wherein the nosepiece comprises a second lens.
  7. The apparatus of claim 6, wherein the second lens comprises a 40X objective.
  8. The apparatus of claim 2, wherein the optical instrument further comprises a specimen identification reader.
  9. The apparatus of claim 7, wherein the specimen identification reader is at least one of a bar code reader and an OCR device.
  10. The apparatus of claim 1, wherein the marker comprises a nib for applying a marking substance to the specimen.
  11. The apparatus of claim 1, wherein the optical instrument is a laboratory microscope.
  12. The apparatus of claim 7, further comprising:

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- a user interface control in electrical communication with the optical instrument; and  
a console in electrical communication with the optical instrument.
13. The apparatus of claim 12, wherein the user interface control comprises:  
at least one input device; and  
a stage positioning device.
  14. The apparatus of claim 13, wherein the stage positioning device comprises a joystick.
  15. The apparatus of claim 13, wherein the at least one input device performs an operation selected from the group consisting of advancing the specimen to a next position in a field of view of the optical instrument, advancing the specimen to a previous position in the field of view, toggling between the first lens and the second lens, and marking an object of interest.
  16. The apparatus of claim 15, wherein the user interface control comprises four input devices, each performing an enumerated operation.
  17. The apparatus of claim 12, wherein the console comprises:  
a keypad; and  
a display.
  18. The apparatus of claim 1, further comprising means for electronically marking an object of interest within the specimen.
  19. The apparatus of claim 18, further comprising an indicator for indicating marked status of field of interest.
  20. The apparatus of claim 19, wherein the indicator comprises:  
an optical path originating at a light source and passing serially through  
the light source;  
a diffuser;  
a mask;  
an aperture;  
focusing optics;  
a lens; and  
a beam splitter, all disposed within a housing.

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21. The apparatus of claim 2, wherein the optical instrument further comprises a sensor for detecting presence of a specimen.
22. The apparatus of claim 21, wherein the sensor is selected from the group consisting of a proximity switch, a limit switch, a hall-effect switch, a magnetic sensor, and an optical sensor.
23. The apparatus of claim 1, wherein the specimen marking system further comprises a cap mechanism coupled to the optical instrument and engageable with the marker.
24. The apparatus of claim 23, wherein the cap mechanism is biased away from the marker when disengaged therefrom and actuatable into an engagement position with the marker by a pin disposed on the stage.
25. The apparatus of claim 23, wherein the cap mechanism includes a resilient seal for sealing a nib of the marker.
26. The apparatus of claim 1 further comprising an actuator for moving the marker relative to the stage.
27. The apparatus of claim 26, wherein the actuator is selected from the group consisting of a solenoid, a motor, and a fluidic cylinder.
28. The apparatus of claim 12 further comprising an audio output device in electrical communication with the optical instrument.
29. A method of marking a specimen, the method comprising the steps of:  
positioning an object of interest within the specimen to a marking position;  
contacting the specimen with a marker; and  
actuating the specimen to create indicia thereon at least partially bounding the object of interest.
30. The method of claim 29, wherein the shape of the indicia is selected from the group consisting of line segments, arcs, and combinations thereof.
31. The method of claim 29, wherein the specimen is disposed on a motorized stage.
32. The method of claim 31, further comprising the step of actuating the motorized stage to position a cap mechanism into an engagement position with the marker.

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33. An automated method of reviewing a specimen, the method comprising the steps of:
- (a) loading the specimen in an optical instrument;
  - (b) locating a first datum mark on the specimen;
  - (c) locating a second datum mark on the specimen;
  - (d) establishing a coordinate system based, at least in part, on the first and second datum marks;
  - (e) positioning the specimen to present a first field of interest;
  - (f) moving to a next field of interest; and
  - (g) repeating step (f) until a predetermined number of fields of interest are presented.

34. The method of claim 33, wherein twenty-two fields of interest are presented.

35. The method of claim 33, wherein the step of moving to a next field of interest includes inputting a user command.

36. The method of claim 33, further comprising the step of electronically marking an object of interest located within the field of interest.

37. The method of claim 36, wherein the step of electronically marking the object of interest includes the steps of:

- inputting a signal to a computer;
- determining if coordinate values for the object of interest are stored as a target zone within the processor; and
- adding the coordinate values of the object of interest to a list of marked target zones, if not previously stored.

38. The method of claim 36, wherein the step of electronically marking the object of interest includes the steps of:

- inputting a signal to a processor;
- determining if coordinate values for the object of interest are stored as a target zone within the processor; and
- removing the coordinate values of the object of interest from a list of marked target zones, if the values are previously stored.

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39. The method of claim 36, further comprising the step of indicating visually a marked status of the object of interest.
40. The method of claim 36, further comprising the step of physically marking an electronically marked object of interest.
41. The method of claim 39, wherein the step of physically marking the electronically marked object of interest comprises:
- inputting a signal to a processor;
  - positioning the object of interest to a marking position;
  - contacting the specimen with a marker; and
  - actuating the specimen to create indicia thereon at least partially bounding the object of interest.
42. The method of claim 33, wherein the step of establishing a coordinate system further comprises:
- centering the first datum mark;
  - assigning a reference coordinate value to the first datum mark;
  - storing in memory the first datum mark coordinate value;
  - centering the second datum mark;
  - assigning a reference coordinate value to the second datum mark;
  - storing in memory the second datum mark coordinate value; and
  - performing a coordinate transformation.
43. The method of claim 42, wherein the step of establishing a coordinate system further comprises comparing the datum mark coordinate values to known parameters to determine if the specimen is loaded in a proper orientation.
44. The method of claim 33 further comprising the step of reading a specimen identifier.
45. The method of claim 44 further comprising the step of accessing a specimen data record stored within the computer to obtain coordinate values for the object of interest.
46. The method of claim 45 further comprising the step of updating the specimen data record to include the coordinate values of the electronically marked objects of interest.

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47. The method of claim 40 further comprising the step of calibrating the marker prior to marking the specimen.
48. The method of claim 47, wherein the step of calibrating the marker comprises:
  - contacting the specimen with the marker;
  - actuating the specimen to create a calibration mark thereon;
  - creating an offset value for the marker by actuating the stage to position the calibration mark into a position relative to the indicia;
  - recording the offset value; and
  - applying the offset value to the marker position.
49. The method of claim 33 further comprising the step performing an autoscan after all fields of interest are presented.
50. The method of claim 40, wherein the marking step is performed after the autoscan step.
51. The method of claim 33, wherein the specimen comprises a cytological material disposed on a slide.
52. The method of claim 51, wherein the specimen is stained with a thionin-phenol solution.
53. The method of claim 52, wherein the thionin-phenol solution comprises a phenol derivative.
54. A method of compensating for vibration errors in an imaging system, the method comprising the steps of :
  - acquiring vibration measurements of the imaging system while scanning portions of a specimen; and
  - re-imaging a portion of the specimen where the vibration measurement for the portion exceeded a predetermined threshold.
55. The method of claim 54 further comprising the step of rejecting the specimen if the vibration measurement for a predetermined number of portions exceed the threshold.
56. The method of claim 54 further comprising the step of rejecting the specimen if the vibration measurement exceeds a second threshold.
57. The method of claim 54, wherein vibration is measured by an accelerometer.

58. The method of claim 57, wherein the accelerometer is disposed on the imaging system.
59. A slide holder assembly comprising:  
a base;  
a first platform movably disposed on the base;  
a second platform disposed on the first platform and including a slide receiving area;  
a slide positioning member operatively connected to the second platform; and  
a mechanism disposed on the base for actuating the slide positioning member.
60. The slide holder assembly of claim 59, wherein the base is coupled to an actuating table.
61. The slide holder assembly of claim 60, wherein the actuating table is coupled to an imaging system.
62. The slide holder assembly of claim 61, further comprising a second slide positioning member operatively connected to the second platform.
63. The slide holder assembly of claim 62, wherein the mechanism comprises a first pin for actuating the first slide positioning member and a second pin for actuating the second slide positioning member.
64. The slide holder assembly of claim 63, further comprising at least one stop disposed on the second platform.
65. The slide holder assembly of claim 64, wherein the first slide positioning member and the second slide positioning member are biased to position a slide disposed in the receiving area into a contact position with the at least one stop.
66. The slide holder assembly of claim 65, wherein the first slide positioning member and the second slide positioning member are biased by a first resilient member and a second resilient member, respectively.
67. The slide holder assembly of claim 66, wherein the first slide positioning member and the second slide positioning member are rotatably mounted to the second platform.
68. The slide holder assembly of claim 63, wherein the first slide positioning member actuates independently of the second slide positioning member.

69. The slide holder assembly of claim 59, further comprising a sensor for detecting presence of a slide disposed in the slide receiving area.

70. The slide holder assembly of claim 69, wherein the sensor is selected from the group consisting of a hall-effect switch, a proximity switch, an optical sensor, and a limit switch.

71. The slide holder assembly of claim 59, wherein the first slide positioning member is a substantially elongate arm having a mounting end and a slide contacting end.

72. The slide holder assembly of claim 62, wherein the second slide positioning member is a substantially elongate arm having a mounting end and a slide contacting end.

73. The slide holder assembly of claim 64, further comprising two stops.

74. The slide holder assembly of claim 63, wherein the first slide positioning member actuates serially with respect to the second slide positioning member.

75. The slide holder assembly of claim 63, wherein the first slide positioning member actuates orthogonally with respect to the second slide positioning member.

76. The slide holder assembly of claim 59, further comprising a slide with a cytological specimen disposed thereon disposed in the slide receiving area.

77. The slide holder assembly of claim 76, wherein the specimen is stained with a thionin-phenol solution.

78. The slide holder assembly of claim 77, wherein the thionin-phenol solution comprises a phenol derivative.

79. An automatic focusing method for an optical system comprising the step of establishing a global focal plane comprising the steps of:

(a) determining an index axis coordinate, a scan axis coordinate, and a focus axis coordinate corresponding to each of three non-collinear locations on a slide; and

(b) determining a numerical representation of the global focal plane using the index axis coordinates, the scan axis coordinates, and the focus axis coordinates.

80. The method according to claim 79, wherein the step of establishing the global focal plane further comprises the steps of:

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- (c) calculating an index axis slope and a scan axis slope;
- (d) determining whether at least one of the index axis slope and the scan axis slope is below a respective corresponding predetermined value; and
- (e) flagging the slide, if at least one of the index axis slope and the scan axis slope is not below the respective corresponding predetermined value.

81. An automatic focusing method for an optical system comprising the step of performing a scan pass comprising the steps of:

- (a) determining a first coordinate that provides a focus value within a predetermined range of an optimal focus value for a first position on a slide substantially corresponding to a first point on a surface substantially corresponding to the surface of the slide;
- (b) moving an element of the optical system relative to the surface of the slide to a position substantially corresponding to the first coordinate; and
- (c) recording the first coordinate corresponding to the first point.

82. The method according to claim 81, wherein the step of performing the scan pass further comprises the steps of:

- (d) determining an area of fine focus jurisdiction surrounding the first point; and
- (e) correlating the first coordinate with the area of fine focus jurisdiction.

83. The method according to claim 82, wherein the area of fine focus jurisdiction is generally elliptical in shape.

84. The method according to claim 83, wherein the area of fine focus jurisdiction has a major axis substantially parallel to a scan axis of the optical system and has a minor axis substantially parallel to an index axis of the optical system.

85. The method according to claim 82, wherein the step of performing the scan pass further comprises the step of:

- (f) determining a second coordinate that provides a focus value within a predetermined range of an optimal focus value for a second position on the slide substantially corresponding to a second point on a surface substantially corresponding to the surface of the slide, comprising the steps of:

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(I) determining whether the second point lies within at least one previously-determined area of fine focus jurisdiction; and

(II) determining an area of fine focus jurisdiction surrounding the second point, if the determination in (I) is negative.

86. The method according to claim 85, wherein step (f) further comprises the steps of:

(III) determining a global focal surface; and

(IV) determining a first estimate of the second coordinate using a representation of the global focal surface.

87. The method according to claim 85, wherein step (f) further comprises the steps of:

(III) determining whether the second point lies within exactly one area of fine focus jurisdiction; and

(IV) retrieving the coordinate correlated with the one area of fine focus jurisdiction, if the determination in (III) is positive.

88. The method according to claim 87, wherein step (f) further comprises the steps of:

(V) determining a global focal surface;

(VI) adjusting the coordinate of step (IV) according to the global focal surface;

and

(VII) moving an element of the optical system relative to the surface of the slide to a position substantially corresponding to the adjusted coordinate of step (VI).

89. The method according to claim 85, wherein step (f) further comprises the steps of:

(III) determining whether the second point lies within more than one area of fine focus jurisdiction; and

(IV) retrieving respective coordinates correlated with each of the more than one areas of fine focus jurisdiction, if the determination in (III) is positive.

90. The method according to claim 89, wherein step (f) further comprises the step of:

(V) using a weighted average of each of the retrieved coordinates based on respective distances of the second point from at least one respective point within each of the more than one areas of fine focus jurisdiction to determine a resultant coordinate.

91. The method according to claim 89, wherein step (f) further comprises the steps of:

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- (V) determining a global focal surface;
- (VI) determining a composite coordinate based on at least one of the retrieved coordinates of step (IV);
- (VII) adjusting the composite coordinate according to the global focal surface; and
- (VIII) moving an element of the optical system relative to the surface of the slide to a position substantially corresponding to the adjusted coordinate of step (VII).

92. The method according to claim 82, wherein the step of performing a scan pass further comprises the step of:

(e) correlating the area of fine focus with a bin that represents a region substantially corresponding to a region on the surface of the slide.

93. The method according to claim 85, wherein the determination in step (I) of whether the second point lies within at least one previously-determined area of fine focus jurisdiction is made by searching only those areas of fine focus jurisdiction which at least partially intersect a bin containing the second point.

94. The method according to claim 82, wherein the step of performing a scan pass further comprises the step of:

(f) determining whether a second position on the slide lies within an area of interest of the slide.

95. An automatic focusing method for an optical system comprising the steps of:

- (a) establishing a global focal surface;
- (b) determining whether a point substantially corresponding to a position located on an area of interest of a slide lies within at least one previously determined area of fine focus jurisdiction;
- (c) determining a coordinate that provides a focus value within a predetermined range of an optimal focus value for the position on the slide;
- (d) imaging a region surrounding the position; and
- (e) repeating at least steps (b) through (d) until substantially all of the area of interest is imaged.

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96. The method according to claim 81, wherein step (b) further comprises moving an element of an optical system relative to the surface of the slide to a position substantially corresponding to the coordinate, and modifying a checksum variable in an amount corresponding to the movement of the element of the optical system.
97. An automatic focusing method for an optical system comprising the step of determining an efficient order of presentation of fields of interest on a slide using an algorithm.
98. The method according to claim 95, wherein the surface of the slide is substantially planar and the slide is of substantially uniform thickness.
99. An automatic focusing method for an optical system comprising the steps of:
- (a) performing an initial coarse focus at a first position substantially corresponding to a first point on a surface substantially corresponding to the surface of a slide; and
  - (b) subsequently performing a plurality of subsequent fine focuses at different positions, wherein each of the fine focuses are performed more quickly than the initial coarse focus.
100. The method according to claim 99, wherein step (a) comprises the steps of:
- (I) imaging the slide at the first position;
  - (II) determining a focus score at the first position;
  - (III) subsequently moving an element of the optical system relative to the surface of the slide by a first amount to a second position;
  - (IV) subsequently imaging the slide at the second position;
  - (V) determining a focus score at the second position;
  - (VI) moving an element of the optical system relative to the surface of the slide by a second amount that is less than the first amount.
101. The method according to claim 99, wherein the fine focuses of step (b) are each performed by imaging a position substantially corresponding to a point on the surface of the slide no more than five times.